substance known as ''chromatin''. In the recent years, more and more evidence has accumulated pointing out chromatin polymorphism and dynamics as a primary mean of control of genome accessibility in time and space, driving the focus on this complex polymer as a critical player in gene regulation. A thorough characterization of chromatin properties would then be a prerequisite step in our understanding of differential gene expression, e.g. ''epigenetics'' in its original definition by Waddington as ''the study of the causal mechanisms by which the genes of the genotypes bring about phenotypic effects''.
We wish here to emphasize some physical characteristics of genome organization in order to provide a more complete framework in which to interpret the control of gene expression. Indeed, as various molecular motors push, pull and twist DNA, transient forces and torques develop within chromatin, with expected consequences on transcription and other DNA metabolism events such as repair or recombination. In addition to discussing some basic mechanical and topological issues, we will also present some recent quantitative and qualitative insights from our lab into chromatin organization and dynamics, including the still controversial role of ions in DNA compaction and the mechanical action of recombinases.
Boulé JB, Mozziconacci J and Lavelle C. (2014). The polymorphism of the chromatin fiber. J Phys Cond Mat (in press).
Lavelle C. (2014). Pack, unpack, bend, twist, pull, push: the physical side of gene expression. Curr Opin Genet Dev 25:74-84.
Huet S, Lavelle C & al. (2014). Relevance and limitations of crowding, fractal, and polymer models to describe nuclear architecture: is a unified picture out of reach? Int Rev Cell Mol Biol 307:443-479.

2718-Pos Board B148
Nucleosome Kinetics and Accesibility of DNA
Jyotsana J. Parmar[1], Dibyendu Das[2], Ranjith Padinhateeri[1].
[1]Biosciences and Bioengineering, Indian Institute of Technology Bombay, Mumbai, India, [2]Physics Department, Indian Institute of Technology Bombay, Mumbai, India.
Crucial cellular processes like gene regulation, transcription, and replication require access to DNA that is covered with nucleosomes. Many experiments suggest that nucleosome organization and dynamics can significantly influence exposure and accessibility of various locations on the genome. In this work we investigate the kinetics of DNA exposure as a result of nucleosome dynamics. We consider binding and dissociation of nucleosomes taking into account both sequence specificity and ATP-dependent activity, and study accessibility of DNA near different kinds of barriers (e.g. a well-positioned protein or a nucleosome free region near transcription start site). Using analytical calculations and numerical simulations, we find the following results. We show that the timescale of exposure of a DNA site near a barrier can be very diverse and crucially depends on the DNA sequence and the initial nucleosome organization. We show how nucleosome-mediated cooperativity can emerge when multiple transcription factors are binding at nearby locations and we investigate how multi-nucleosome correlations influence the time scale of accessibility as a function of the distance from the barrier. We discuss ramifications of our findings in understanding gene regulation and stochasticity in gene expression.

2719-Pos Board B149
Chromosome-Nuclear Envelope Interactions Have Multiple Effects on Chromosome Folding Dynamics in Simulation
Nicholas A. Kinney[1], Igor V. Sharakhov[2], Alexey V. Onufriev[3].
[1]Genomics, Bioinformatics, and Computational Biology, Virginia Tech, Blacksburg, VA, USA, [2]Entomology, Virginia Tech, Blacksburg, VA, USA, [3]Computer Science, Virginia Tech, Blacksburg, VA, USA.
It is well recognized that the chromosomes of eukaryotes fold into non-random configurations within the nucleus. In humans and fruit flies, chromosomes likely adopt a particular 3D configuration called the fractal globule (FG) which has multiple biologically significant properties. However, the fractal globule is a metastable state which, over time, transitions to a less biologically favorable state called the equilibrium globule. One of the key questions is how the FG state is stabilized in-vivo? We use simulations to study the effects of chromosome-nuclear envelope (Chr-NE) interactions on the dynamics of the fractal globule within a model of Drosophila melanogaster (fruit fly) interphase chromosomes. The computational model represents chromosomes as self-avoiding walks (SAW) bounded by the nuclear envelope (NE). Model parameters such as nucleus size, chromosome persistence length, and chromosome-nuclear envelope interactions are taken directly from experiment. Several key characteristics of the non-equilibrium FG state are monitored during each simulation's progress: chromosome territories, intra-chromosomal interaction probabilities, loci specific diffusion constants, and presence of the Rabl (polarized) chromosome arrangement. Next, we compare the outcomes of simulations which include or exclude Chr-NE interactions. We find that Chr-NE interactions reinforce the non-equilibrium properties such as chromosome territories, high intra-chromosome interaction probabilities, and the Rabl chromosome arrangement. In addition, Chr-NE interactions affect loci specific and averaged chromosomal diffusion. Based on these results we conclude that the presence of Chr-NE interactions may delay the decay of the biologically relevant fractal globule state in vivo.

2720-Pos Board B150
Biophysical Models of Nucleosome Positioning
Razvan V. Chereji, David D. Clark.
NICHD, National Institutes of Health, Bethesda, MD, USA.
A human body contains enough DNA to circle the Earth's Equator more than 2.5 million times. The basic units of DNA packaging are called nucleosomes. Their locations along the chromosomes play an essential role in gene regulation. We study nucleosome positioning in yeast, fly and mouse, and build biophysical models in order to explain the genome-wide nucleosome organization. We show that DNA sequence is not the major cause of the regular arrays of nucleosomes observed in vivo near the transcription start sites (TSS). We construct a minimal model in which nucleosomes are positioned by potential barriers located in the gene promoters, and which accurately reproduces the genome-wide nucleosome occupancy patterns observed over the transcribed regions in living cells. Our statistical mechanics model allows us to study nucleosome phasing against potential barriers and wells [1, 2], sequence-dependent nucleosome affinity [2], nucleosome unwrapping [3], competition between different DNA-binding proteins, and accessibility of transcription factors [4, 5] to target sites which are found in nucleosomal DNA, among others. We also discuss alternative nucleosome positioning mechanisms: nucleosome anchoring [6] and active nucleosome positioning by ATP-dependent remodelers [7].
[1] RV Chereji, D Tolkunov, G Locke, AV Morozov, Phys. Rev. E 83, 050903 (2011)
[2] RV Chereji and AV Morozov, J. Stat. Phys. 144, 379 (2011)
[3] RV Chereji and AV Morozov, Proc. Natl. Acad. Sci. U.S.A. 111, 5236 (2014)
[4] N Petrenko, RV Chereji, MN McClean, AV Morozov, JR Broach Mol. Biol. Cell 24, 2045 (2013)
[5] N Elfving*, RV Chereji*, V Bharatula, S Björklund, AV Morozov, JR Broach, Nucleic Acids Res. 42, 5468 (2014) (* contributed equally)
[6] RV Chereji, AV Morozov, YM Moshkin, in preparation
[7] D Ganguli*, RV Chereji*, J Iben, HA Cole, DJ Clark, Genome Res. (2014) (* contributed equally)

2721-Pos Board B151
Prediction of Chromosome Conformations with Maximum Entropy Principle
Bin Zhang, Peter G. Wolynes.
Rice University, Houston, TX, USA.
The genomes' three-dimensional (3D) organization is crucial in regulating many biological processes, including gene regulation, DNA replication, and cell differentiation. A high-resolution chromosome structure thus will significantly advance our understanding of these important processes. A major step toward building a structural model of the chromosome is the inventions of chromosome conformation capture methods, 5C and Hi-C, that aim at detecting physical contact frequencies between pairs of genomic loci. However, computational approaches to construct 3D structures that are consistent with these experimental contact frequency measurements remain lacking.
We develop a statistically rigorous approach based on maximum entropy principle to determine a least-biased potential energy landscape that reproduces experimentally determined Hi-C contact frequency between genome pairs. The resulting energy landscape supports a knotless chromosome conformation, which has been highly anticipated since complex knotted conformations prohibit the access of gene information for transcription and hinder DNA replication. We further show that the topologically associating domain signal alone also enforces a chromosome structure free of knots. Our results highlight the importance of local interactions in determining the global topology of the chromosome structure. Finally, the derived landscapes for multiple chromosomes support the formation of territories that have long been observed in microscopy experiments. Together with Hi-C experiments, our approach provides a coherent picture of the 3D architecture of the genomes that is consistent with many the available experimental data.

2722-Pos Board B152
Modeling the Binding of H-NS to DNA
Eva C. van Mastbergen, **Jocelyne Vreede**.
van 't Hoff Institute for Molecular Sciences, University of Amsterdam, Amsterdam, Netherlands.
Bacterial chromosomal DNA is organized within a structure called the nucleoid, which is distinctly different from the rest of the cytoplasm. Bacteria have a number of nucleoid-associated proteins that influence the organization of the